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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/486,293 | 08/22/2000 | JONATHAN A COOPER | 14538A-004010US | 3432 |

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| EXAMINER | |
|---|---|
| GEBREYESUS, KAGNEW H | |
| ART UNIT | PAPER NUMBER |
| 1652 | |

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/486,293 | COOPER ET AL. | |
| | Examiner | Art Unit | |
| | Kagnew H. Gebreyesus | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *19-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. Applicant's election of Claims 1-18 in part and polynucleotide encoding the protein of SEQ ID NO: 3 in the reply filed on January 21, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant is reminded that division of groups A-C is a restriction and not an election of species thus the argument that additional species will be considered is not agreed to and the restriction is proper and made final.

Claims 19-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected groups, there being no allowable or linking claims.

### *Claim Objections*

1. Claim 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 18 must depend on a preceding independent claim not on a proceeding claim. For examination purposes claim 18 depends on claim 13.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 5-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 5-9 are rejected over the recitation "Hybridize" or "specifically hybridize" without a statement of the conditions used.

***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-10 and 13-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not contain any disclosure of the structure of all DNA sequences of all mammalian mDab1 and fragments thereof. The genus of polynucleotides that encode polypeptides that comprise any mammalian Dab1 or any fragment thereof, is a large variable genus with the potentiality of encoding many different proteins from any mammalian source. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences and sequences that have not been disclosed by the specification. The specification discloses only a few (three) species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus including any polynucleotide encoding any polypeptide with

the sole limitation of having a phosphotyrosine binding domain and being capable of associating with Src, Abl or Fyn as there are other genes encoding polypeptides such as e.g. p62 or SLM-1 with these attributes but are unrelated to mDab1. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1-3, 5-12 and 13-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA sequence of SEQ ID NO: 3, does not reasonably provide enablement for any fragment thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-3, 5-12 and 13-17 are so broad as to encompass any fragment of a polynucleotide encoding a phosphotyrosine domain containing peptide from any mammalian species. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides encoding functionally unrelated phosphotyrosine domain containing polypeptides capable of associating with Src, Abl or Fyn broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed

knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to SEQ ID NO: 3 or the phosphotyrosine-binding domain therein.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any polynucleotide that will hybridize to SEQ ID NO: 2, any ortholog, allelic or splice variant of the polypeptide of SEQ ID NO: 3 encoded by SEQ ID NO: 2, as well as any polynucleotide having 60%-95% identity to SEQ ID NO: 2 because the specification does **not** establish: (A) regions of the polynucleotide sequence which may be modified without necessarily affecting the protein structure necessary for it's ability to specifically associate with Src, Abl or Fyn; (B) the general tolerance of the polynucleotide encoding the specific mDab1 to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any segment of the polynucleotide encoding mDab1 with an expectation of retaining the capacity to associate with Src, Abl or Fyn; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the

claims broadly including mammalian Dab1 Disabled protein 1, or a fragment thereof. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any fragment of mDab1 retaining the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2, 5, 6, 7 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonaldo et. al. Bonaldo et. al. teach a sequence that shows 100% identity to residues spanning nucleotide 53 - 658 of SEQ ID NO: 2 encoding the protein of SEQ ID NO: 3. Claim 1 and 2 encompass SEQ ID NO: 3 and fragments thereof, therefor are anticipated by Bonaldo's sequence. Claims 5 is anticipated since Bonaldo's sequence can hybridize to SEQ ID NO: 3. Claims 7 and 9 are drawn to any sequence that comprises 15-60 nucleotides within SEQ ID NO: 3 therefor are anticipated by Bonaldo's sequence.

*Claim Rejections - 35 USC § 102*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 1- 5 are rejected under 35 U.S.C. 102(a) as being anticipated by Howell et. al. (Genbank accession Y08379). Howell et. al. teach a murine dab1 protein that comprises a sequence that is identical to that set forth IN SEQ ID NO: 3. This sequence first appeared in the GenBank database on January 08, 1997.

6. Claims 1- 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Howell et. al. Howell et. al., teach ( in a published journal article by "Mouse disabled (mDab1): a Src binding protein implicated in neuronal development" EMBO journal Vol.16 No.1 pp121-132, 1997) isolated polynucleotides encoding mDabl, splice variants ( anticipating claims 1-5), probes used in northern hybridization (anticipating claims 6-9) as well as vectors comprising said polynucleotides (anticipating claims 10, 11) and host cells transformed with said vectors (anticipating claims 12-17) to express mDabl proteins. (See Fig 3 and Materials and Methods on page 129). Therefor, Howell et al. anticipates all the claims 1-18.

*Claim Rejections - 35 USC § 103*

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 5 and 6-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaldo et. al. above. Given that claim 1-3 recite fragments of SEQ ID NO: 2 and claims 6-9 recite a probe without disclosure of a specific sequence or the position within SEQ ID NO: 2 thereto it would have been obvious for a person of ordinary skill in the art to make a probe or use Bonaldo's sequence or fragment thereof for purposes of hybridizing (claim 5) to SEQ ID NO: 2 to detect or identify homologous sequences (claims 6-9). It would also have been obvious to insert Bonaldo's sequence in an expression vector (claims 10-17) in order to produce a peptide that can be used to produce an antibody probe for the protein encoded by the full length gene. The many advantages of recombinant production of useful proteins are well known within the art as are recombinant methods of obtaining the necessary genes. These advantages include the

ability to produce much larger quantities of the protein, being able to produce the protein in more easily handled organisms, reducing the number of steps necessary for the purification of a protein and producing the protein in a purer form by using an organism that does not include naturally occurring contaminants of the protein. As such the disclosure of a useful protein, such as that of Bonaldo's et al. clearly suggests to the ordinary skilled artisan a gene encoding for the protein would be useful to produce large quantities of the protein. Therefore, it would have been obvious to one of ordinary skill in the art to isolate and express the gene encoding the mDab1 of Bonaldo et al. using well known recombinant methods for the isolation of such genes, insertion of the isolated gene into an expression vector, transformation into a suitable host and expression of the encoded protein.

9. Claims 6-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howell et. al. Howell et. al. (Genbank accession Y08379). Howell et. al. teach a murine dab1 protein that comprises a sequence that is identical to that set forth in SEQ ID NO: 3. This sequence first appeared in the GenBank database on January 08, 1997. Given that this sequence is 100% identical to the sequence disclosed by current applicants it would have been obvious for a person of ordinary skill in the art to make a probe (claims 6-9) or use Howell's sequence or fragment thereof for purposes of hybridizing (claims 5 to SEQ ID NO: 2) to detect or identify homologous sequences. It would also have been obvious to insert Howell's sequence in an expression vector, transform such vector in a cell (claims 13-18) in order to express the protein of SEQ ID NO 3.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy ponnathapura can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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